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Dr. Joshua Lederberg,
Stanford University School of Medicine,
Dept. of Genetics,
300 Pasteur Drive,
Palo Alto, California,
U.S.A.

Dear Josh,

I have not yet seen Holley's paper in Science, but I think I follow most of what you say.

It is an old speculation that the S-RNA is so big because it may have to make a rather nicely balanced configurational change. However, it was assumed that this would come about when the amino acid was added. Your idea that it will only happen when the S-RNA combines with the correct codon is new to me.

I don't feel that there is anything hard to explain about the "Bernfield-Nirenberg" binding. You only have to assume that in addition to the binding energy between the codon and the anti-codon there is a weak general binding of S-RNA and codon to the ribosomes. I suspect that the binding between the codon and the anti-codon without the ribosome is too weak to be observable at all easily.

Basically I think your idea a good one, but it may be hard to prove it.

Yours ever,
Francis

F. H. C. Crick

Crick